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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,086	03/26/2001	Dale Baskin	7414.0043	2844

22852 7590 03/12/2007

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EXAMINER
TUNG, JOYCE

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
03/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/818,086	Applicant(s) BASKIN ET AL.	
	Examiner Joyce Tung	Art Unit 1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 16 January 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *26-50*.
   Claim(s) withdrawn from consideration: *51-67*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: please see the attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☒ Other: interview summary on 3/6/07.

The applicant's response filed 1/16/07 to the Office action has been entered. Claims 26-67 are pending.

1. Claims 26, 28-35, 39-40, 43-45 and 47-50 remain rejected under 35 U.S.C. 102(e) as being anticipated by Wittwer et al. (6,174,670, issued January 16, 2001).

Wittwer et al. disclose the method of monitoring hybridization during polymerase chain reaction using of double stranded DNA dye or specific hybridization probes and quantitating amplified DNA (See the Abstract). The invention of Wittwer et al. includes a method of detecting a difference at a selected locus in a first nucleic acid as compared to a second nucleic acid (See column 8, lines 35-37). The method comprises providing a pair of primer for amplification by polymerase chain reaction and an oligonucleotide probe, wherein one of the primers and the probe are each labeled with one member of a fluorescence energy transfer pair comprising an donor fluorophore and an acceptor fluorophore (See column 8, lines 38-58). The selected segment of first nucleic acid and the corresponding segment of the second nucleic acid are amplified by polymerase chain reaction in the presence of effective amounts of primers and probe to result in an amplified selected segment and an amplified corresponding segment, at least a portion of having the labeled primer and probe hybridized thereto with fluorogenic resonance energy transfer pair in resonance energy transfer relationship (See column 8, lines 59-67). The amplified segments are illuminated, fluorescence emission is measured by a device (See column 22, lines 59-66), the first melting profile of the probe melting from the amplified selected segment of the first nucleic acid and a second melting profile of the probe melting from the amplified selected segment of the second nucleic acid are determined. The first melting profile to the second melting profile is compared to determine the differences between these segments (See

column 9, lines 1-15). The fluorescent indicator is SYBR™ Green I, ethidium bromide (See column 22, lines 54-56) and a 5'-nuclease probe (See column 17, lines 22-26). The nucleic acid is from human genomic DNA (See column 26, lines 29-30).

Wittwer et al. do not explicitly disclose combining nucleic acid from the sample with at least one set of reaction composition comprising a first reaction composition and second reaction composition, both specific for the at least one target polynucleotide, wherein the first reaction composition comprises amplification primers specific to at least one target polynucleotide and the second reaction composition comprises a fluorescent indicator and amplification primers specific to at least one target polynucleotide.

Wittwer et al. disclose that three fluorescence-monitoring techniques for PCR are performed. Each reaction composition has a pair of primers and a fluorescence indictor (See column 32, lines 28-61). It is inherent in this teaching that the nucleic acid sample combined at least one set of reaction compositions comprising a first reaction composition and second reaction composition, both specific for the at least one target polynucleotide, wherein the first reaction composition comprises amplification primers specific to at least one target polynucleotide and the second reaction composition comprises a fluorescent indicator and amplification primers specific to at least one target polynucleotide. Thus the teachings of Wittwer et al. anticipate the limitations of the claims.

The response argues that Wittwer et al. fail to disclose the first reaction composition has no fluorescent indicator and the determining step recited as that whether the at least one amplification product is present in both the first reaction composition and the second reaction

composition from the intensity of signal from the fluorescent indicator in the second reaction composition.

However, since the method of the instant claims is described by using open language "comprising" to describe the components of the first composition and the method steps, it is inherent that the first composition could have any components to fulfill the method and in the irradiating step, the first composition could be irradiated and in monitoring step the first composition could be monitored. Therefore, based upon the teachings of Wittwer et al. the teachings of Wittwer et al. anticipate the limitations of the claims (See column 32, lines 28-61, fig. 47). Thus, the rejection is maintained.

As discussed in the interview on 3/6/07, it is suggested to amend language to exclude a fluorescent indicator used in the first composition, and the first composition, which is not irradiated and monitored for overcoming the 102(e) rejection.

2. Claims 27, 36-38 and 41-42 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wittwer et al. (6,174,670, issued January 16, 2001) as applied to claims 26, 28-35, 39-40, 43-45 and 47-50 above, and further in view of Johston-Dow et al. (6,103,465, issued August 15, 2000).

The teachings of Wittwer et al. are set forth in section 1 above. Wittwer et al do not disclose a nucleic acid sequencing reaction on the amplification product, the source of DNA sample used as listed in claims 36-38 and determining at least one HLA type.

Johnston-Dow et al. disclose a method for typing HLA class I gene and the method involving DNA sequencing techniques (See the Abstract and column 9, lines 9-22). The method is to provide for the specific DNA sequencing of HLA-A, HLA-B and HLA-C (See column 3,

lines 19-22). Johnston-Dow et al. also disclose that any source of human nucleic acid can be used, for example, blood and lymphoblostoid cell lines (See column 6, lines 9-14) as recited in the limitations of claim 50. Johnston-Dow et al. further indicate that HLA typing is performed routinely in connection with many medical indications, the study of auto-immune disease and the determination of susceptibility to infectious disease (See column 1, lines 57-62). This teaching suggests the limitations of claims 36-38 in that the pathogen will be from a virus, prokaryote and eukaryote, the presence of the given target polynucleotide indicates the presence of the genetic disease or a specific allele which can indicate serotype.

It would have been prima facie obvious to an ordinary skill in the art at the time of the instant invention to apply the sequencing method of Johnston-Dow et al. because the method of Johnson-Dow et al. is applied to the locus-specific nucleic acid amplification followed by sequence-specific detection of the amplified product for the DNA typing of HLA class I gene via DNA sequencing in that by sequencing the exons in both directions, the effect of sequencing errors on the assignment of HLA type is minimized and the method greatly reduces the number of reagents and the complexity of the sequencing protocols required (See column 9, lines 29-37).

The response argues the same issue as discussed above in connection with claim 26 that "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition..." As discussed in section 1, with the same reasons as set forth in section 1, the rejection is maintained.

2. Claim 46 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Wittwer et al. (6,174,670, issued January 16, 2001) as applied to claims 26, 28-35, 39-40, 43-45 and 47-50 above, and further in view of Lukhtanov et al. (6,790,945, issued September 14, 2004).

The teachings of Wittwer et al. are set forth in section 1 above. Wittwer et al. do not disclose using a minor groove binding molecule as a fluorescent indicator.

Lukhtanov et al. disclose oligonucleotide probes containing a minor groove binding molecule (See the abstract). The invention relates to oligonucleotide-quencher-fluorescent-dye conjugates having improved characteristics and to reagents suitable for incorporating novel quencher and fluorescent dye moieties into oligonucleotide (See column 1, lines 1-18 and column 4, lines 46-57).

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply the minor groove binding molecule of Lukhtamov et al. because Lukhtamov et al. indicate that the reagents used for labeling oligonucleotide overcome the unfavorable characteristics (See column 4, lines 28-30), for example, mixtures are difficult to separate or unstable during oligonucleotide synthesis or having overlapping emission wavelengths with other desirable reporters (See column 4, lines 24-27). It would have been prima facie obvious to

have minor groove binding molecule as a fluorescent indicator for determining the presence and sequence of at least one target polynucleotide in a sample.

The response argues the same issue as discussed above in connection with claim 26 that "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition..."

As discussed in section 1 above, with the same reasons as set forth in section 1, the rejection is maintained.

Summary

4. No claims are allowable.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung
March 6, 2007

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

3/7/07